REMARKS

Claims 1-8, 13, 14, 17-20, and 22-25 are currently pending in the application. Claims 1-3, 5-7, 13, 17, 22, and 23 are amended. Claim 26 is added. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

The Examiner notes that although Applicant had indicated in the previous response that Claims 1-8 and 13-25 were pending, but that claims 15, 16, and 21 were cancelled in Applicant's response of February 28, 2003. The Examiner is correct, and Applicant has indicated claims 15, 16, and 21 above as being cancelled.

Rejection of Claims 1-8, 13-14, 17-20, and 22-25 Under 35 U.S.C. §103(a)

The Examiner has rejected claims 1-8, 13-14, 17-20, and 22-25 under 35 U.S.C. §103(a) as being unpatentable over Hiserodt et al. in view of the "known fact" disclosed in the Specification on pages 52-54 and 66-68.

Hiserodt et al. teach vaccine compositions. Specifically, Hiserodt et al. teach that "[m]inimally, the vaccines of this invention comprise two components. The first is a source of tumor antigen...[t]he second component is a **cytokine producing cell**" (col. 7, 1-9; emphasis added). Hiserodt et al. teach that the "cytokine producing cell" can be a cell from an allogenic donor "that has been genetically altered to express the cytokine at an elevated level" (col. 7, 10-14), or that the "cytokine producing cell" is a cell that is autologous or syngenic to the patient "that has been genetically altered to produce a cytokine" (col. 7, 18-21). The specific embodiments taught by Hiserodt et al. have been detailed in Applicant's previous responses and do not need to be repeated here, other than to emphasize that every embodiment of vaccine composition taught by Hiserodt et al. includes a cell which has been genetically modified to produce cytokine.

Applicants consider that the claims, as amended, traverse the rejection. Hiserodt et al. either alone or in conjunction with the "known fact" do not teach or suggest *all the claim limitations*. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974). In addition, there is no suggestion or motivation, either in the references themselves or in the knowledge generally

available to one of ordinary skill in the art, to modify the reference or to combine reference teachings (*In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)).

Even if combined, the asserted prior art do not teach or suggest all the limitations of the amended claims.

The claims of the instant application have been amended without prejudice to refer specifically to a subclass of the invention disclosed in the specification, namely, compositions which are substantially free of cells genetically modified to produce cytokine. Unlike the compositions currently claimed, the compositions taught by Hiserodt et al. are based entirely on the presence of genetically modified cytokine producing cells. Without cytokine producing cells, the vaccine compositions taught by Hiserodt et al. would contain no cytokine at all. That is, Hiserodt et al. do not teach a composition comprising a cell and an engineered cytokine where the composition is substantially free of cells that have been genetically modified to produce cytokine.

The "known fact" referred to by the Examiner does not remedy the deficiency in the teachings of Hiserodt et al. The "known fact" merely teaches that the technical know-how for coupling a cytokine to a lipid was available in the art at the time the application was filed. With respect to the Examiner's assertion that the "known fact" also provides that it was conventional in the art to produce an opsonin-enhanced cell to allow more efficient binding, engulfment, and internalization of the antigen, Applicant respectfully disagrees. The specification teaches that "*it is believed that* opsonin-enhanced cells provide a beneficial effect *according to the invention* because the opsonin portion acts as a link or coupling agent between the antigen and the APC to allow more efficient binding, engulfment, and internalization of the antigen" (p. 51, lines 27-30; emphasis added). This is not a statement of what was conventional in the art at the time of filing, but a statement relating to a hypothesized mechanism of action of a component of the invention. This statement is not an admission of what was known in the art, but a portion of the disclosure of **the invention**; this "known fact" is not prior art. In addition, the opsonin-enhanced cell claims depend from claim 1, and thus, also require a composition comprising a cell to which is bound an exogenous, engineered cytokine, and substantially free of cells genetically modified to

produce cytokine; this is not taught by Hiserodt et al. Moreover, neither of the "known facts" indicated by the examiner teach a composition which is substantially free of cells genetically modified to produce cytokine. Whether considered alone or together, Hiserodt et al. and the "known fact" do not teach all of the elements of the claimed invention. On this ground alone, the amended claims should be found non-obvious over Hiserodt et al. and the "known fact".

There is no motivation to modify the teachings of Hiserodt et al. to arrive at the claimed invention.

In order to render the claimed invention obvious, there must be some motivation combine the references asserted and/or modify the teachings therein to arrive at the claimed invention (*In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)). There is no motivation in the teachings of Hiserodt et al., the "known fact" relating to lipid linked cytokines, or the general knowledge of those of skill in the art which would suggest to one of skill in the art to modify the teachings of Hiserodt et al. to produce the claimed method. Every embodiment disclosed by Hiserodt et al. is drawn to the use of cells which are genetically modified to produce cytokine. There is no teaching or suggestion in Hiserodt et al. relating to a cellular vaccine in which the cytokine is not produced by the cells of the vaccine; that is, Hiserodt et al. does not teach or suggest a composition which is substantially free of cells that have been genetically modified to produce cytokine. In fact, cytokine producing cells are the **only** source of cytokine in the compositions taught by Hiserodt et al. The "known fact" only teaches that the technical know-how to link a cytokine to a lipid was known in the art at the time of filing. The only disclosure of compositions for stimulating an immune response which are substantially free of cells genetically modified to produce cytokine comes from Applicant's description of the invention, and this is not useable as a source of motivation to reach a finding of obviousness. *In re McLaughlin*, 443 F.2d 1392 (CCPA 1971).

The claims of the instant invention which, in addition to the compositions of claims 1 and 13, include an opsonin-enhanced cell are, likewise, not obvious over the teachings of Hiserodt et al. and the "known fact". Because the invention of claims 1 and 13 are novel and non-obvious over the teachings of Hiserodt et al. and the "known fact" the combination of the subject matter

of claims 1 and 13 with an opsonin-enhanced cell is necessarily non-obvious over the teachings of Hiserodt et al. and the known fact.

Accordingly, Applicant requests that the rejection under 35 U.S.C. §103 be reconsidered and withdrawn.

Applicant submits that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicant's attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney/agent of record.

Respectfully submitted,

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